IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket: WALLACH=16A

In re Application of:	)	Conf. No.: 2547
David WALLACH et al	)	Art Unit: 1642
Appln. No.: 09/824,134	)	Examiner: M. Davis
Filed: April 3, 2001	)	Washington, D.C.
For: MODULATORS OF THE FUNCTION OF FAS/APO1 ...	)	January 22, 2007

REPLY BRIEF

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Randolph Building, Mail Stop Appeal Brief - Patents
401 Dulany Street
Alexandria, VA 22314

Sir:

The present reply brief is responsive to the examiner's answer of November 21, 2006, and is in full accordance with 37 C.F.R. 41.41.

The Examiner's Indefiniteness Argument Ignores The Teachings Of The Prior Art

In the examiner's discussion of the 35 U.S.C. 112, second paragraph, rejection for indefiniteness of the language "moderately stringent conditions" and in her rebuttal to appellant's arguments with respect to this rejection, the

examiner improperly ignores the guidelines of MPEP §2173.02, quoted at pages 10 and 11 of appellant's appeal brief. The most significant section is where it states:

> Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and
>
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

In the paragraph bridging pages 17 and 18 of the examiner's answer, the examiner stated:

> Since there is no definition of moderately stringent hybridization conditions in the instant specification, and since "moderate" is a relative term, one of ordinary skill in the art cannot determine the metes and bound of the claimed invention.

In this analysis, it is apparent that the examiner is ignoring appellant's argument that the content of the application disclosure is but one piece of information that must be analyzed, along with the teachings of the prior art and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. Indeed, there are cases that find terms definite that are not even used in the specification; see, for

example, *Bancorp Services, L.L.C. v. The. Hartford Life Ins. Co.*, 359 F.3d 1367, 1372, 69 USPQ2d 1996, 1999-2000 (Fed. Cir. 2004), discussed in MPEP §2173.02. This case stands for the proposition that even a claim term that is not used or defined in the specification may not be indefinite if the meaning of the claim is discernable. The court held that the phrase "surrender value protected investment credits" was not indefinite despite the fact that it was not defined or even used in the specification, because "the components of the term have well recognized meanings, which allow the reader to infer the meaning of the entire phrase with reasonable confidence."

In appellant's main brief, many pieces of prior art are cited which use the term "moderate stringency" with respect to DNA hybridization as in the context of the present claims. This prior art is reasonably consistent with respect to the meaning of this terminology. It is urged that the Board take Official Notice of the fact that the level of skill in the art of molecular biology is extremely high. Patent disclosures are supposed to begin at the level of skill in the art and not disclose everything that is already known in the art.

Here, the term "moderate stringency" is used in the specification, although it is not defined in the present specification. However, the term has a known definition when

considering the teachings of the prior art and, thus, the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made is that interpretation that is required by the definitions known in the art to those of ordinary skill in the art, i.e., conditions that allow detection of nucleotide sequences at least approximately 75% homologous to the probe. All of this is meticulously explained in appellant's main brief.

The examiner has not discussed the prior art material cited by appellant to show that the definition of this term can be reasonably inferred by one of ordinary skill in the art. The examiner merely makes attorney argument that the particular definitions cited by appellant "would be just one of possible numerous reasonable interpretations of the instantly claimed moderately stringent hybridization conditions" (see page 18 of the examiner's answer). However, the examiner has not drawn the Board's attention to any other reasonable interpretation other than that discussed in appellant's main brief. The examiner appears to rely entirely on the fact that there is no definition in the specification. This is an improper standard. Accordingly, reversal of the examiner and withdrawal of the indefiniteness rejection is respectfully urged.

With Respect To the Written Description Rejection the Examiner Improperly Incorporates the Indefiniteness Rejection

At page 7 of the examiner's answer, in the discussion of the written rejection (35 U.S.C. 112, first paragraph) rejection, the examiner states:

> Due to the indefinite language of "hybridization under moderately stringent conditions", which is a relative term, supra, a DNA sequence hybridizing under moderately stringent conditions with the DNA sequence encoding SEQ ID NO:2 encodes a peptide or protein of any size, and unknown structure, wherein said peptide or protein does not have to share a substantial sequence homology with SEQ ID NO:2.

It is thus clear that the examiner's reasoning with respect to written description is intertwined with the examiner's reasoning as to why the claims are indefinite. However, the definiteness rejection is a separate rejection. If the claims are found to be unpatentable for failure to comply with the second paragraph of 35 U.S.C. 112, then it is irrelevant whether or not they comply with the first paragraph of 35 U.S.C. 112. Accordingly, for the purpose of appellant's analysis of the 35 U.S.C. 112, first paragraph, written description, rejection, appellant will assume that the 35 U.S.C. 112, second paragraph rejection has been overcome for the reasons argued with respect thereto in appellant's main brief and herein. Thus, the "moderately stringent" language

must be interpreted as one of ordinary skill in the art would infer in light of the prior art and the specification as a whole, that is, requiring conditions that would result in the DNA having at least about 75% homology to the probe.

When accepting the definiteness of the language "hybridization under moderately stringent conditions" with the definition urged by appellant, the examiner's argument falls. The analogs do not encompass peptides or proteins "of any size, and unknown structure, wherein said peptide or protein does not have to share a substantial sequence homology with SEQ ID NO:2" (examiner's answer, page 7). The DNA sequence of claim 1(2) must have at least 75% homology to the cDNA encoding SEQ ID NO:2, and it must bind with the intracellular domain of the FAS ligand receptor (FAS-IC). Thus, any peptide encoded by such a DNA and which binds to FAS-IC must share a substantial sequence homology with SEQ ID NO:2, by definition. Thus, it is not "unknown structure". The examiner is effectively reading out "moderately stringent conditions" and taking the position that the claim can read on peptides that are totally irrelevant to SEQ ID NO:2 and happen to bind to FAS-IC. This is simply not the case as any reasonable interpretation of the term "moderately stringent conditions" requires substantial homology to SEQ ID NO:2. Once it is understood that the claims do not encompass sequences of

"unknown structure", i.e., having no structural relationship to SEQ ID NO:2, all of the examiner's reasoning becomes irrelevant.

Binding To FAS-IC Is A Definitive Function

Beginning at the bottom of page 8, of the examiner's answer, the examiner states that "binding to FAS-IC by itself is not a definitive function." The examiner then states that binding alone is not sufficient for the property of activation of FAS ligand receptor or the property of displacing the binding of FAS ligand to its receptor. However, this statement is irrelevant. The claims do not require that the DNA thereof encode peptides that have the property of activation of FAS ligand receptor or the property of displacing the binding of FAS ligand to its receptor. The claims only require that peptides bind to FAS-IC. A utility for such peptides is in affinity chromatography to isolate FAS-IC, or the entire FAS protein, by binding to FAS-IC. At page 21 of the examiner's answer, the examiner disregards this alleged utility stating:

> Moreover, concerning applicant's new arguments that binding alone is sufficient to establish the function of serving the affinity chromatograph to isolate … FAS-IC protein, it is noted that the encompassed genus of analogs could bind to FAS-IC with

> **any** affinity, for example, with extremely low affinity, and thus the proteins, that bind to the affinity column made of the claimed analogs, do not necessarily have any effect or correlation with SEQ ID NO:2 (MORT-1), or FAS-IC protein.
>
> The specification however **does not disclose which structure of the claimed genus of analogs has sufficient affinity**, such that they could be used for affinity chromatograph to isolate FAS-IC or FAS receptor, other than SEQ ID NO:2 and its amino acids 153-215 or 130-245 of SEQ ID NO:2. [emphasis original]

It is thus apparent that the examiner interprets the requirement of claim 1(2) that the analog "binds with the intracellular domain of the FAS ligand receptor (FAS-IC)" as reading on analogs that bind with infinitesimal affinity, thus effectively negating this limitation. However, no limitation of the claim can be ignored or simply interpreted out of the claim altogether. Those of ordinary skill in the art would not interpret the term "binds with … FAS-IC" as comprehending infinitesimal affinity or affinity so low that it will not retain any FAS-IC when a composition containing FAS-IC is passed thru an affinity chromatography column. Even relatively low affinity binding must result in some amount of FAS-IC being retained on the column and therefore such analogs are useful. They only have no use when they will not retain any FAS-IC and in that case it cannot reasonably be said that such analog "binds with FAS-IC." The present specification

includes disclosure of binding assays; see for example page 34, lines 3-13. Those of ordinary skill in the art reading the claims in light of the specification would understand that in order to determine whether any given analog binds to FAS-IC, there must be an affinity sufficient that it is able to test positive in a standard binding assay, such as that disclosed in the specification. If they can be identified by such a binding assay, then they can be used for affinity chromatography. The examiner's interpretation is simply unreasonable.

As binding with FAS-IC is in itself a reasonable utility in order to isolate FAS-IC, all of the examiner's comments about alternative utilities in the specification, such as inducing cytotoxicity or inhibiting FAS-induced cytotoxicity, should be ignored.

As all of the other points made by the examiner are based on the incorrect notion that the term "moderately stringent conditions" does not require any structural similarity between analog and probe, all of these additional arguments must also be disregarded. For all of these reasons and the reasons explained in appellant's main brief, reversal of the examiner and withdrawal of the rejection under the 35 U.S.C. 112, first paragraph, written description requirement are respectfully urged.

As To The Enablement Rejection, The Examiner Err In Requiring That The Specification Be Enabling For Proteins With *In Vivo* Utility

At page 13, the last paragraph, the examiner states with respect to the 35 U.S.C. 112, first paragraph, "scope" (enablement) rejection:

> One cannot extrapolate the teaching in the specification to the claims, because one cannot predict which of the encoding analogs, or the encoded fragments of SEQ ID NO:2 that bind with FAS-IC, would have the property of SEQ ID NO:2, such as activation of cytotoxicity, or the property of the C-terminal amino acids 130-245 of SEQ ID NO:2, such as inhibition of SA-induced cytotoxicity, to have any practical, real world use.

At page 15, the examiner again states:

> In view of the above, one would not know how to make the claimed DNA sequences encoding analogs or fragments of SEQ ID NO:2 that bind to FAS-IC, such that they would be of any practical use, such as activation of cytotoxicity or inhibition of FAS-induced cytotoxicity.

Again, in the paragraph bridging pages 27 and 28 of the examiner's answer, the examiner states:

> One cannot predict among those analogs that bind to FAS-IC, which mutant or which fragments of SEQ ID NO:2 would bind to FAS-IC with sufficient affinity and having necessary conformation to have practical use, which use defines and distinguishes the claimed invention from others; e.g., inducing cytotoxicity, or inhibitng FAS-

> induced cytotoxicity, because of the unpredictability of protein chemistry, as taught by Burgess et al, Lazar et al, Tao et al, and Gillies et al, which applies as well to DNA sequences that encode proteins.

It is thus apparent that the examiner, in order to support this rejection, is reading something into the claim that is not there. The examiner believes that the only real world utilities disclosed are *in vivo* utilities, such as inducing cytotoxicity or inhibiting FAS-induced cytotoxicity. However, as already discussed above, the claims do not require such utility. The claims are directed to DNA and the use of such DNA to make a polypeptide that binds to FAS-IC. As discussed above, binding to FAS-IC is in and of itself a sufficient practical real world utility, as it can be used, for example, in affinity chromatography in order to isolate FAS-IC or the entire FAS-protein, which isolated proteins are known to have utility. By failing to recognize this valid *in vitro* utility, the examiner's entire enablement argument becomes irrelevant to the language of the claim as properly interpreted in light of the present specification.

As discussed above, the language "binds with" cannot be interpreted so broadly as to effectively vitiate the requirement of binding. The present specification includes disclosure of binding assays; see for example page 34, lines 3-13. Those of ordinary skill in the art reading the claims

in light of the specification would understand that in order to determine whether any given analog binds to FAS-IC, there must be an affinity sufficient that it is able to test positive in a standard binding assay, such as that disclosed in the specification. If they can be identified by such a binding assay, then they can be used for affinity chromatography.

Whether or not it would take undue experimentation to find those analogs that induce cytotoxicity or inhibit FAS-induced cytotoxicity is irrelevant. It is not an issue in this appeal. The issue is whether it would take undue experimentation to find analogs that bind to FAS-IC. That can be done with standard assays with high throughput and would not involve undue experimentation any more than the binding assays considered *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), i.e., the binding of antibody to a specific substrate. The examiner has not rebutted appellant's position as stated in appellant's main brief that finding analogs with at least 75% homology to SEQ ID NO:2 and that bind to FAS-IC would not take undue experimentation.

The Examiner's Other Arguments Relating To The Enablement Rejection Are Untenable

At page 13, the examiner states:

> The claimed DNA sequences encode a genus of analogs, which encompass a genus of peptide or protein ligands of unknown structure, that bind to FAS-IC with any binding affinity, ranging from very low affinity to very high binding affinity, such as peptide mimetics, any agonist, antagonist, wherein the structure [of] said ligands do not have to be substantially similar to that of SEQ ID NO:2, or its C-terminal amino acids 130-245.

It is apparent from this statement that the scope rejection relies substantially on the examiner's interpretation of "moderately stringent conditions" as being so indefinite that it must encompass any conditions, such that the claim will read on absolutely any DNA that encodes a peptide that binds to FAS-IC having absolutely no structural similarity to SEQ ID NO:2. As discussed above, this is an improper interpretation of the claim language. The language "moderately stringent conditions" requires that the DNA sequence encoding the analogs must have at least 75% homology to the sequence encoding SEQ ID NO:2. Thus, the claims require substantial structural similarity to SEQ ID NO:2 and do not read on any totally unrelated peptide mimetic, agonist, antagonist, etc.

At the bottom of page 14 of the examiner's answer, the examiner states:

> Further, the claims encompass polynucleotides comprising non-disclosed nucleic acid sequences attached to a

> polynucleotide that encode a peptide fragment that binds to FAS-IC; that is polynucleotides that hybridize to said polynucleotides under the undefined moderately stringent conditions.

This new argument of the examiner is not fully understood. While the preamble of claim 1 uses the term "comprising" the DNA sequence of 1(2) must be present. That sequence may be fused to a different sequence, but the DNA sequence of 1(2) must be present in the claimed isolated DNA molecule. The sequence of claim 1(2) must both be capable of hybridization to cDNA encoding SEQ ID NO:2 under moderately stringent conditions and it must encode an analog that binds with FAS-IC. Thus, this simply does not read on binding analogs that do not have substantial structural similarity to SEQ ID NO:2.

At pages 34 and 35, the examiner relies on *Rochester v. Searle*, 358 F.3d 916, Fed Cir, 2004, for the position that screening assays are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention. However, the fact situation in the *Rochester* case is substantially different from that present here. In *Rochester*, the inventors had disclosed absolutely no protein having the desired functional property. The screening assay was to find currently unknown proteins having a certain function. The proteins were defined entirely by function and this was found to be improper by the *Rochester*

court. Here, however, the specification discloses SEQ ID NO:2, which is a protein having the desired function. Furthermore, all of the analogs of SEQ ID NO:2 now claimed must have substantial similarity to SEQ ID NO:2. As discussed above, in order for a DNA sequence that encodes such an analog to hybridize to cDNA encoding SEQ ID NO:2 under moderately stringent conditions, there must be at least 75% sequence homology. The specification teaches how to make mutations in SEQ ID NO:2, test them for binding under moderately stringent conditions, and then screen in a simple binding assay for binding to FAS-IC. Thus, the full scope of the analogs of the present claims is supported by an enabling disclosure and the holding with respect to the fact situation in *Rochester* is irrelevant to the present situation.

For all of the reasons presented herein, in conjunction with the reasons explained in appellant's main brief, reversal of the examiner and withdrawal of the 35 U.S.C. 112, first paragraph, "scope" rejection is respectfully urged.

CONCLUSION

All of the claims now presented for appeal fully comply with 35 U.S.C. 112. Reversal of the examiner and

allowance of all of said claims are therefore earnestly solicited.

Respectfully submitted,

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